Session III

Free Radical Mechanisms in Neurodegenerative Disorders- A Common Pathogenesis?

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CNS SOURCES OF REACTIVE OXYGEN SPECIES

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Although it is clear that the CNS can undergo damage by exposure to reactive oxidant species (ROS), the source of the damaging molecules is not always evident. A variety of potential sources of both reactive oxygen and reactive nitrogen species exist, including auto-oxidation of molecules, the leakage of ROS from the electron transport chain and the action of specific enzymes. One potentially important source of reactive oxidants which has been overlooked is the CNS macrophage, the microglia. Like other tissue macrophages, the microglia generate ROS as part of their normal function. The release of ROS by microglia is important to the CNS for two primary reasons-1) microglia are distributed in a matrix-like arrangement throughout all regions of the CNS and 2) the generation of reactive oxidants by microglia is induced during injury and inflammation. Microglia, therefore, not only generate significant quantities of reactive oxidants but are also in an ideal position to promote oxidative changes in neurons and other glia.

In order to understand how microglia contribute to changes in the oxidative environment of the CNS, we have examined the regulation of superoxide anion and NO production by microglia cultured from rodent and human CNS. Microglia from all species studied release superoxide anion but not necessarily NO and minimal difference is seen between cultured adult and cultured neonatal microglia. Preliminary data from hippocampal brain slice further suggests that production of ROS occurs *in vivo* as well as *in vitro*.

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